

Serial No.: 08/612,929  
Group Art Unit No.: 1806

Please amend claims 1 - 2, 4 - 11, 14, 16, 30 - 32 and 37 as follows:

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B1  
a1

1. (Amended) A fusion protein having binding specificity for human interleukin-4 (IL4) [which comprises] comprising:  
six complementarity determining regions (CDRs), [derived] wherein said six CDRs include three heavy chain CDRs and three light chain CDRs and at least one of said CDRs is obtained from a non-human neutralizing monoclonal antibody [characterized by] having a dissociation constant equal to or less than  $2 \times 10^{-10}$  M for human IL4, and  
a first protein or peptide encoded by a first fusion partner.

2. (Amended) The fusion protein according to claim 1 [which] wherein said first protein or peptide is operatively linked to a second protein or peptide encoded by a second fusion partner.

4. (Amended) The fusion protein according to claim 2 wherein said second fusion partner comprises [all or part of] a component selected from the group consisting of an immunoglobulin constant heavy chain, [or] an immunoglobulin constant light chain, [or] and both.

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B2

5. (Amended) The fusion protein according to claim 1 wherein said first protein comprises [fusion partner sequence is the heavy chain sequence of:] amino acids 21-50, 56-71, 88-119, and 131-141 of SEQ ID NO: 12 sequentially.

6. (Amended) The fusion protein according to claim 1 wherein said first protein comprises [fusion partner sequence is the light chain sequence of:] amino acids 20-42, 58-72, 80-111, and 121-131 of SEQ ID NO: 14 sequentially.

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7. (Amended) The fusion protein according to claim 1 wherein a first of said heavy chain CDRs is [said amino acid sequences of the complementarity determining regions for the heavy chain are:

(a)] ThrSerGlyMetGlyValSer: SEQ ID NO:22,  
a second of said heavy chain CDRs is

[(b)] HisIleTyrTrpAspAspAspLysArgTyrAsnProSerLeuLysSer: SEQ ID NO:24, [or

(c)] and a third of said heavy chain CDRs is ArgGluThrValPheTyrTrpPheAspVal: SEQ ID NO:26.

ad cont  
8. (Amended) The fusion protein according to claim 1 wherein a first of said light chain CDRs is ~~[said amino acid sequences of the complementarity determining regions for the light chain are:~~

~~[(a)]~~ ~~[Leu]~~LysAlaSerGlnSerValAspTyrAspGlyAspSerTyrMetAsn: SEQ ID NO:16,  
~~[(b)]~~ a second of said light chain CDRs is AlaAlaSerAsnLeuGluSer: SEQ ID NO:18, ~~for~~  
~~[(c)]~~ and a third of said light chain CDRs is GlnGlnSerAsnGluAspProProArg: SEQ ID NO:28.

9. (Amended) The fusion protein according to claim 1 wherein a first of said light chain CDRs is ~~[said amino acid sequences of the complementarity determining regions for the light chain are:~~

~~[(a)]~~ LysAlaSerGlnSerValAspTyrAspGlyAspSerTyrMetAsn: SEQ ID NO:16,  
~~[(b)]~~ a second of said light chain CDRs is AlaAlaSerAsnLeuGluSer: SEQ ID NO:18, ~~for~~  
~~[(c)]~~ and a third of said light chain CDRs is GlnGlnSerAsnGluAspProProThr: SEQ ID NO:20.

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10. (Amended) An immunoglobulin heavy chain complementarity determining region (CDR), the amino acid sequence of which is selected from the group consisting of:

~~[(a) ThrSerGlyMetGlyValSer: SEQ ID NO:22,]~~

~~[(b)]~~ a) HisIleTyrTrpAspAspAspLysArgTyrAsnProSerLeuLysSer: SEQ ID NO:24, and

~~[(c)]~~ b) ArgGluThrValPheTyrTrpPheAspVal: SEQ ID NO:26.

11. (Amended) An immunoglobulin light chain complementarity determining region (CDR), the amino acid sequence of which is selected from the group consisting of:

~~[(a) LeuAlaSerGlnSerValAspTyrAspGlyAspSerTyrMetAsn: SEQ ID NO:16,~~

~~(b) AlaAlaSerAsnLeuGluSer: SEQ ID NO:18,]~~

~~[(c)]~~ a) GlnGlnSerAsnGluAspProProArg: SEQ ID NO:28; and

~~[(d)]~~ b) GlnGlnSerAsnGluAspProProThr: SEQ ID NO:20.

14. (Amended) A humanized antibody comprising a heavy chain and a light chain, said antibody [characterized by] having a dissociation constant equal to or less than about  $2 \times 10^{-10}$  M for human IL4, wherein the framework regions of said heavy and light chains are [derived] obtained from at least one selected human antibody and the amino acid sequences of the complementarity determining regions of each said chain are [derived] obtained from a non-human neutralizing monoclonal antibody specific for human IL4 [characterized by] having a dissociation constant equal to or less than about  $2 \times 10^{-10}$  M for human IL4.

16. (Amended) A chimeric antibody comprising a heavy chain and a light chain, said antibody [characterized by] having a dissociation constant equal to or less than about  $2 \times 10^{-10}$  M for human IL4, wherein the amino acid sequences of the complementarity determining regions of said heavy chain and said light chain are derived from a non-human neutralizing monoclonal

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antibody specific for human IL4 [characterized by] having a dissociation constant equal to or less than about  $2 \times 10^{-10}$  M for human IL4.

30. (Amended) A method for [diagnosing allergies and other conditions associated with] detecting excess immunoglobulin E production in a human which comprises contacting a sample of biological fluid with a high titer monoclonal antibody for human IL4 and assaying for the occurrence of binding between said monoclonal antibody and human interleukin 4.

31. (Amended) A method for screening monoclonal antibodies which have a high titer for human interleukin 4 which comprises:

- a) preparing a hybridoma cell line characterized by secretion of a monoclonal antibody to human interleukin 4; and
- b) screening said hybridoma cell line with aldehyde[-coupled] labeled human interleukin-4 or biotinylated human interleukin-4, wherein said human interleukin-4 is not denatured.

32. (Amended) ~~A neutralizing monoclonal antibody having a high titer for human interleukin-4, a Fab fragment or a F(ab')<sub>2</sub> fragment thereof, produced by screening a library of hydridoma products with aldehyde[-coupled] labeled human interleukin-4 or biotinylated human interleukin-4.~~

37. (Amended) The monoclonal antibody according to claim 36 [having the identifying characteristics of] wherein said monoclonal antibody is 6A1.